PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 163501.0 DAB	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/IL2005/001279	International filing date *(day/month/year)* 30.11.2005	Priority date *(day/month/year)* 02.12.2004
International Patent Classification (IPC) or national classification and IPC INV. G01N33/564		
Applicant CAN-FITE BIOPHARAMA LTD. et al.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 2 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
28.09.2006	14.03.2007
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized officer Rosin, Oliver Telephone No. +31 70 340-8925

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/IL2005/001279

Box No. I Basis of the report

1. With regard to the **language**, this report is based on

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3(a) and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4(a))
   - ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages	
1-19	as originally filed
Claims, Numbers	
1-13	filed with telefax on 19.02.2007
Drawings, Sheets	
1/9-9/9	as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☒ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☒ the claims, Nos. 14-20
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-13
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-13
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-13
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The application is new because it is not known in the prior art that the effectiveness of an anti-inflammatory treatment of a subject comprises determining the expression levels of an A3 adenosine receptor (A3AR) agonist in peripheral mononuclear cells (PBMNC) from the subject in two or more successive time points, at least one of which is during an anti-inflammatory treatment, wherein a difference in the level being indicative of effectiveness of the drug treatment.

The subject matter of independent claim 1 is therefore novel (Art 33(2) PCT).

It was also not known that a method for selecting a subject suffering from a certain inflammatory disease to receive anti-inflammatory therapeutic treatment comprises determining the level of expression of A3AR in the PBMNC of the subject and selecting the subject to receive said anti-inflammatory treatment if said level is above a predetermined level.

The subject matter of independent claim 8 is therefore novel (Art 33(2) PCT).

Assessment of inventiveness.

The closest prior art document D1 describes a method of determining an inflammatory state by determining the level of A3AR in cells "obtained from the blood" (par [0040]).

The additional technical feature of the application over the closest prior art is the determination of the effectiveness of an anti-inflammatory treatment of a subject and that this determination includes measurements in two or more successive time points, especially in PBMNC.

The effect of this feature is the selection of a special cellular fraction indicative for effectiveness of anti-inflammatory treatment.

The problem that is solved by the application is "how to provide a method of determining

the effectiveness of an anti-inflammatory treatment".

There is no teaching in the prior art that solves this problem. Therefore the current application is inventive.

Claims 1-13 are industrial applicable (Art 33(4) PCT.

CLAIMS:

1. A method for determining the effectiveness of an anti-inflammatory therapeutic treatment of a subject, the treatment comprising administering an A_3 adenosine receptor (A_3AR) agonist to the subject, comprising determining the expression level of A_3AR in peripheral blood mononuclear cells (PBMNC) from the subject, in two or more successive time points, at least one of which is during an anti-inflammatory treatment, wherein a difference in the level being indicative of effectiveness of the drug treatment.

2. The method of Claim 1, wherein one or more first samples are taken at a time point prior to initiation of the treatment and one or more second samples are taken at a time point during the treatment, wherein a decrease in the level of the A_3AR expression in the one or more second samples as compared to the one or more first samples is indicative that the treatment is effective.

3. The method of Claim 1, wherein one or more first samples are taken at a time point during the treatment and one or more second samples are taken at a time point during the treatment subsequent to the time point of the one or more first samples, wherein a decrease in the level of the A_3AR expression in the one or more second samples as compared to the one or more first samples is indicative that the treatment is effective.

4. The method of Claim 1, wherein one or more first samples are taken at a time point during the treatment and one or more second samples are taken at a time point after the treatment has been discontinued, wherein an increase in the level of the A_3AR expression in the one or more second samples as compared to the one or more first samples is indicative that the treatment is effective.

5. The method of Claim 1, wherein said therapeutic treatment involves an anti-inflammatory drug.

6. The method of Claim 1, wherein the inflammatory state is the result of an autoimmune disease.

7. The method of Claim 6, wherein the autoimmune disease is rheumatoid arthritis (RA).

8. A method for selecting a subject suffering from a certain inflammatory disease, to receive anti-inflammatory therapeutic treatment that comprises administering to the subject A_3AR agonist, the method comprising determining the level of expression of A_3AR in the PBMNC of the subject and selecting the subject to receive said anti-inflammatory therapeutic treatment if said level is above a predetermined level.

9. The method of Claim 8, wherein said sample of PBMNC is taken from a subject before receiving an anti-inflammatory treatment.

10. The method of Claim 9, wherein the inflammatory state is the result of an autoimmune disease.

11. The method of Claim 10, wherein the autoimmune disease is rheumatoid arthritis (RA).

12. The method of Claim 9, wherein said anti-inflammatory therapeutic treatment comprises providing said subject with an anti-inflammatory amount of IB-MECA.

13. The method of Claim 9, for selecting a candidate for receiving anti-inflammatory therapeutic treatment under clinical studies.